Supplementary Materials

Supplementary Figure S1. Mean leukocyte telomere length (LTL) trends by age and genotype for variants of *APOE*. Telomere length was assessed using Southern blot analysis of terminal restriction fragment size (15). Regression analysis of LTL versus participant age for *APOE* alleles (n=121; *ε3*/*ε3*=94, *ε2*/*ε2* & *ε2*/*ε3*=9, *ε4*/*ε4* & *ε4*/*ε3*=6). No significant differences were observed by genotype ($p>0.10$).

Supplementary Figure S2. Leukocyte telomerase activity in carriers and non-carriers of the protective *FOXO3* variant. Both telomere length and telomerase activity were assessed in the same blood samples. Telomerase activity was measured using the TRAP assay (n = 87 [*TT* = 42, *G*-allele carriers = 45]). No significant difference in telomerase activity (mean ± SE) was found between carriers and non-carriers of the protective *FOXO3 G*-allele ($p > 0.10$ by Student's *t*-test).

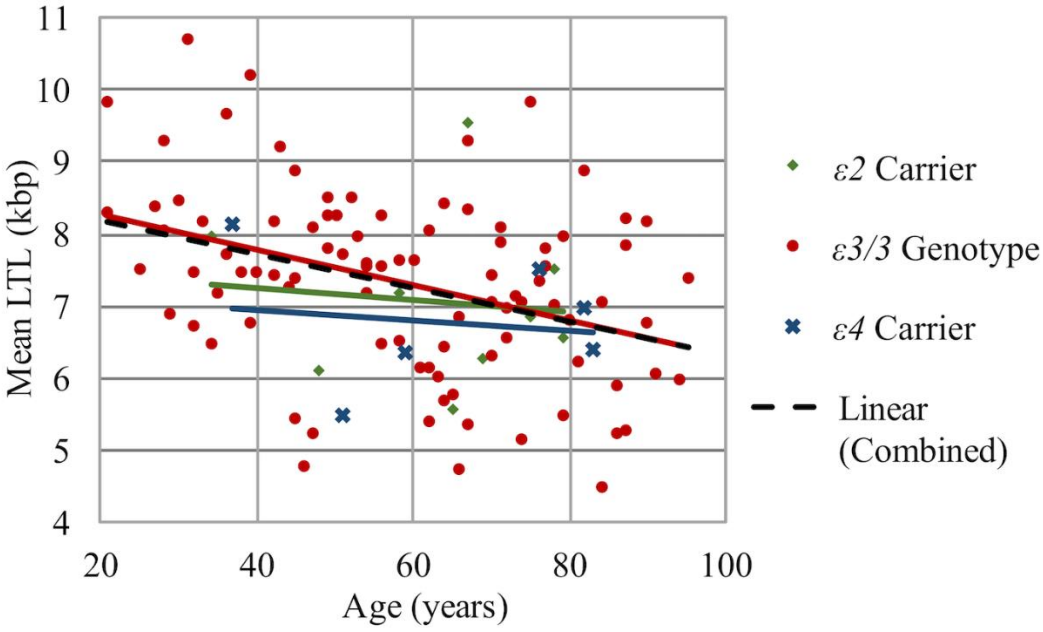
Supplemental Methods. *APOE* genotyping was performed by standard PCR amplification, followed by restriction enzyme digestion and gel electrophoresis of the products to identify the three individual alleles. Briefly, 35 PCR cycles were performed using 50 ng of genomic DNA per reaction mixture that included the following primers at a final concentration of 500 nM; F4 5'-GACGCGGGCACGGCTGTCCAAGGAG-3' and F6 5'-CCCTCGCGGGCCCCGGCCTGGTACAC-3'. The PCR product was digested with the restriction endonuclease *Hha*I for 2 h at 37°C then resolved on a 4% agarose gel in 1 x sodium borate buffer.

Genotyping of the *FOXO3 rs2802292* SNP variants was performed using amplification-refractory mutation system allele-specific PCR. One hundred nanograms of genomic DNA was amplified using the following primers; forward outer ("rs2802292_FO"), 5'-GAAACTGAGGCTAACAGCTGGGTCTGGCCC-3', reverse outer ("rs2802292_RO"), 5'-AGCTGATGCTCCTCAACGAAACCACCTTAC-3', reverse *G*-specific ("rs2802292_RG"), 5'-GGACCCCTTCATCTGTCACACAGAGGCTC<u>C</u>-3', and forward *T*-specific ("rs2802292_FT"), 5'-CTGTTGCTCACAAGAGCTCAGGGCTGGGC<u>T</u>-3', at a final concentration of 1 μM

for the outer primers and 500 nM for the allele-specific primers. Following 30 cycles of PCR, the products were resolved on a 3% agarose gel in 1 x sodium borate buffer.

For telomere length analysis, genomic DNA extracted from peripheral blood mononuclear cells was digested with restriction enzymes *Hin*fI and *Rsa*I at 37°C. One and a half micrograms of restriction enzyme-digested DNA were resolved in 0.5% agarose gels and Tris-borate-EDTA buffer with radiolabeled DNA standards. Southern blotting was performed with a radio-labeled telomere-specific oligonucleotide (24 bp), followed by exposure to a storage-phosphor screen and scanning with a Typhoon 9500 (GE) laser scanner to visualize the telomere restriction fragments. Leucocyte telomere length (LTL) was assessed by measuring mean terminal restriction fragment length using Quantity One software (Bio-Rad), with bp lengths calibrated to radiolabeled standards. Telomerase activity was assessed using the TRAPeze kit following manufacturer's guidelines with the following modifications. The CHAPS extract equivalent of 1 x 10^4 cells was used per reaction and CHAPS extract of freshly collected PBMC was used as a standard. Quantification of TRAP assay products was made using ImageQuant software version 5.1 (GE).

Supplemental Figure 1.



Supplemental Figure 2.